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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/848,820	05/19/2004	Timothy A. McKinsey	MYOG:044US	4787

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FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

EXAMINER	
PETERSEN, CLARK D	
ART UNIT	**PAPER NUMBER**
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/848,820	MCKINSEY ET AL.	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-89 and 100* is/are pending in the application.

4a) Of the above claim(s) *19-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-18 and 100, in the reply filed on 12 December 2006 is acknowledged.

Additionally Applicants' election of the species of staurosporine for Group A, Intravenous or oral administration for Group B, beta blocker for Group C, and increased cardiac output for Group D, is acknowledged.

Claims 19-89 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 December 2006.

Drawings

The drawings are objected to because Fig. 6A is too dark to convey any information. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the

brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 and 100 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: Claims 1-18 and 100 are directed to identifying patients suffering from or at risk of developing hypertrophy or heart failure, and treating these patients with regimens involving protein kinase D (PKD) inhibitors to prevent or ameliorate their symptoms.

Breadth of the claims: The claims are broad in that they are drawn to a method of treating with a wide range of known kinase inhibitors (see claim 2, for example). Additionally, claims 12-18 are drawn to preventing cardiac hypertrophy entirely by administration of one inhibitor selected from a large group of inhibitors recited (see claim 13, for example).

Guidance of the specification and existence of working examples: The specification provides examples of transgenic mice in which PKD regulation has been altered such that PKD activity is enhanced versus wild-type mice, and the correlation of overexpression with cardiac dilation (see Brief Description of the Drawings, Figs. 7A-D, pp. 12-13 of the instant specification, for example). Additionally the specification provides extensive hypothetical descriptions of pharmacological agents that could conceivably be used to modulate various signaling pathways involved in the progression of cardiac hypertrophy (see pp. 17-47 of the instant specification). However there are no working examples detailing how various agents were administered to any mammalian patient suffering from or predicted to suffer from cardiac hypertrophy, only the Figs. 7A-D demonstrating that PKD overexpression can cause the disease. There is no guidance as to effective amounts to administer or protocols or regimens for treating the disease as recited in the instant claims.

Predictability and state of the art: Administration of drugs such as beta blockers and staurosporine are routinely administered *in vivo* for treatment of numerous conditions or for experimental study of various physiological phenomena. Their use is well known in the art.

Amount of experimentation necessary: Although administration of drugs such as beta blockers and staurosporine are well known in the art, their effective combination for treating or preventing cardiac hypertrophy is not described. Because the instant specification also does not include an example protocol, rather only general hypothetical arguments that their administration would be beneficial, it is deemed that the reduction of the current invention to practice would require undue experimentation on the part of one of ordinary skill in the art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-18 and 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Buchholz et al (Hypertension, 1991), in light of Bing et al (Jan 2002). Buchholz et al teach a method of administering staurosporine to spontaneously hypertensive rats. Hypertension is known as a risk factor for hypertrophy, therefore selection of these rats reads on identifying a patient at risk

of hypertrophy. Additionally spontaneously hypertrophic rats are well characterized as developing hypertrophy in response to their hypertensive disease (see Bing et al, 2002). They teach that one can administer staurosporine to rats intravenously and record arterial pressure and cardiovascular activity (see p. 93, col. 2, for example). They also administer staurosporine by gavage, reading on oral administration (see p. 93, col. 2, for example). They administer a second therapeutic, namely the beta blocker nadolol, to rats 5 min before intravenous administration of staurosporine. They teach that this combination lowers mean arterial pressure and decreases tachycardia (see Fig. 5, p. 97; see text, p. 95 last paragraph to p. 96, col. 1, as examples). Because spontaneously hypertensive rats are bred to exhibit a hypertensive phenotype, their use reads on claims 17 and 18 in which the patient has a genetic predisposition and familial history for hypertension. The methods taught by Buchholz et al inherently have the results cited in claim 100.

Bing et al teach that the spontaneously hypertensive rat is an ideal model for studying heart failure and hypertrophy as it applies to human disease (see Abstract, p. 71, col. 1, for example). They teach that that it is normal practice to measure heart failure and heart improvement through measurements of cardiac output such as ejection fraction (see Introduction, p. 71, col. 2 for example). Additionally they teach that it is possible to measure changes in ejection fraction in spontaneously hypertensive rats approaching heart failure; they also teach that mortality is a useful parameter for measuring cardiac response to drug treatment (see "Prevention and Treatment of Heart Failure", p. 76, for example).

Therefore the teachings of Buchholz et al, in light of the teachings of Bing et al, are deemed to anticipate the instant claims 1-6, 8-18, and 100.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-18 and 100 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buchholz et al.

The teachings of Buchholz et al are discussed above and applied as before.

Regarding the limitation of claim 7 that administration of a beta blocker occurs simultaneously with staurosporine, it would be an obvious matter of convenience to the artisan whether to administer the drugs simultaneously or five min apart.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer staurosporine and beta blockers in a method of treating cardiac hypertrophy and failure simultaneously in a method of treating or preventing cardiac hypertrophy or cardiac failure.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP
2/23/2007

JON WEBER
SUPERVISORY PATENT EXAMINER